

Topics in Primary Care Medicine

The Alcohol-Withdrawal Syndrome

CHARLES G. BROWN, MD, *Baltimore*

"Topics in Primary Care Medicine" presents articles on common diagnostic or therapeutic problems encountered in primary care practice. Physicians interested in contributing to the series are encouraged to contact the series' editors.

—BERNARD LO, MD
STEPHEN J. MCPHEE, MD
Series' Editors

The syndrome of alcohol withdrawal is characterized by tremulousness, hallucinations, seizures and delirium following withdrawal from ethanol. The severity of the withdrawal syndrome depends on both the amount and the duration of ethanol consumption. The syndrome can be precipitated at any time during which the blood ethanol concentration decreases. Therefore, not only cessation but a reduction in the intake of ethanol can precipitate the withdrawal syndrome. Some patients consume smaller quantities of ethanol but concurrently take other sedative-hypnotic agents (barbiturates, benzodiazepines) that are cross-tolerant with ethanol. A syndrome similar to ethanol withdrawal can also be precipitated if one of the sedative-hypnotics is withdrawn.

Clinical Presentation

The alcohol-withdrawal syndrome can be divided into four clinical stages. During stage 1 (six to eight hours after the cessation of ethanol intake), signs and symptoms of autonomic hyperactivity predominate. Most patients experience tremulousness and anxiety. On physical examination tachycardia, hypertension, diaphoresis and hyperreflexia are often found. In addition, a patient may be easily startled, and there may be a craving for alcohol or other sedative-hypnotic drugs.

In stage 2 (about 24 hours after ethanol cessation), hallucinations occur and accompany the autonomic hyperactivity of stage 1. The hallucinations are usually auditory or visual but may be tactile, olfactory or mixed.

The hallmark of stage 3 is the appearance of grand mal seizures. The overwhelming majority of patients who have seizures do so within 7 to 48 hours after the

cessation of ethanol intake. Most patients will have two to six seizures in a six- to eight-hour course. The seizures are brief and a patient usually has a relatively short postictal period. About 30 percent to 40 percent of untreated patients who have seizures during ethanol withdrawal will go on to have delirium tremens.

Stage 4 of the ethanol-withdrawal syndrome is characterized by autonomic hyperactivity, hallucinations and global confusion (delirium tremens). The occurrence of seizures after the onset of delirium tremens is distinctly unusual. This stage begins some 72 hours after cessation of ethanol intake, but can be seen as late as 14 days. In only about 6 percent of patients who withdraw from alcohol do the symptoms, if untreated, progress to this stage.

It appears that patients who are at greatest risk for delirium tremens developing will have either temperatures above 40°C (104°F) or fluid or electrolyte disturbances. Complications include aspiration, trauma and vascular collapse. Mortality from delirium tremens is still estimated at 15 percent to 25 percent.

Pathophysiology

While no satisfactory pathophysiologic explanation for the alcohol-withdrawal syndrome exists, clinical experience has shown that in patients who are tolerant to "toxic" levels of ethanol some compensatory physiologic mechanism must develop that opposes ethanol's depressant effects. When blood ethanol concentrations begin to decrease, these compensatory mechanisms become unopposed and appear clinically as autonomic hyperexcitability (that is, tremor, hypertension, tachycardia and hyperreflexia). In addition, hypomagnesemia

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From the Division of Emergency Medicine and Trauma, Department of Emergency Medicine, The Johns Hopkins Hospital, Baltimore.

Reprint requests to Charles G. Brown, MD, Associate Director, Division of Emergency Medicine and Trauma, Department of Emergency Medicine, The Johns Hopkins Hospital, 600 N Wolfe Street, Baltimore, MD 21205.

and hypokalemia may be factors in the development of the withdrawal syndrome.

Differential Diagnosis

The tremor of alcohol withdrawal poses little difficulty in determining differential diagnosis, especially when there are other autonomic signs and symptoms and a history of recent cessation of ethanol intake. The tremor of alcohol withdrawal is postural and therefore maximal when a patient's arms are outstretched. It is a fairly rhythmic tremor that oscillates at about six to eight cycles per second and worsens with agitation. Another postural tremor seen in this patient population is asterixis. This occurs with a metabolic encephalopathy (for example, hepatic failure) and is more intermittent and irregular than the tremor of alcohol withdrawal. Cerebellar tremors, which can be seen with alcoholic cerebellar degeneration or as part of Wernicke's syndrome, worsen with movement and abate at rest, and therefore are easily distinguished from postural tremors.

The hallucinations seen during stage 2 of ethanol withdrawal need to be differentiated from alcoholic hallucinosis, an alcohol-related toxic psychosis. The differentiation is made on the basis of time of onset, presence of autonomic signs and symptoms and the type of hallucination. With alcoholic hallucinosis the onset of the hallucination begins within 72 to 96 hours after the cessation of ethanol intake and is not characterized by the presence of autonomic hyperexcitability as occurs in ethanol withdrawal. The hallucinations of alcoholic hallucinosis are usually auditory. In ethanol withdrawal, auditory hallucinations as well as visual, tactile and olfactory hallucinations may occur.

Seizures seen during ethanol withdrawal are classically grand mal and short-lived. As mentioned, most patients have two to six seizures in about an eight-hour time course. A greater number of seizures—or seizures occurring past this time course—should alert a physician to consider other causes.

With the initial presentation of seizures during alcohol withdrawal, the differentiation from idiopathic seizures is at times quite difficult. If electroencephalography can be done, this may aid in the differential diagnosis. In patients with alcohol-withdrawal seizures, an electroencephalogram may show abnormalities during a seizure, but the findings should return to normal shortly following it. In patients with an underlying seizure disorder, electroencephalographic abnormalities are present both during the seizure and after recovery.

Status epilepticus is quite unusual during ethanol withdrawal and should suggest other causes, including withdrawal of short-acting barbiturates and central nervous system infections. Focal seizures seen during ethanol withdrawal suggest an underlying structural lesion such as subdural hematoma, subdural empyema, intracerebral hemorrhage, cerebrovascular disease, arteriovenous malformation or tumor.

The appearance of delirium within the context of the withdrawal syndrome presents little diagnostic chal-

lenge. When it is the initial presentation, other disorders should be considered including central nervous system and systemic infections, as well as thyrotoxicosis and hypoglycemia.

In many patients who have chronic alcoholism and who are admitted to hospital for such problems as gastrointestinal bleeding, trauma, pneumonia or hepatic decompensation, signs and symptoms of alcohol withdrawal may develop during their hospital stay. Therefore any alteration in vital signs, mental state or manifestations of seizure activity must be viewed with this in mind.

Treatment

In the early stages of alcohol withdrawal the objectives of treatment should be to allay symptoms and to halt the progression of the withdrawal syndrome. Although reinstitution of alcohol intake is probably one of the most widely used forms of "self-treatment" its short duration of action and the metabolic disturbances that result from its consumption make this an inappropriate treatment modality. Several other sedative-hypnotic agents, which are cross-tolerant with ethanol, are more effective in abating the autonomic hyperactivity and suppressing the hallucinations.

One useful sedative-hypnotic is paraldehyde. It is effective in dosages of 10 ml by mouth every two to three hours. It should not be used intramuscularly because it may cause sterile abscesses, or per rectum because it may also cause a regional proctitis. Although its odor might be considered a detracting factor, this also tends to lower its abuse potential.

Other drugs that may be effective during these early stages include diazepam, chlordiazepoxide and oxazepam. In patients who have hepatic disease or hypoproteinemia, administration of diazepam and chlordiazepoxide must be cautiously regulated because both these drugs have pharmacologically active metabolites that are protein bound. Therefore, in patients being aggressively treated by the administration of these drugs the cumulative effects of the drugs' metabolites on the patients' level of consciousness must be monitored. Oxazepam does not pose this problem as it is metabolized to an inactive form. Because of this, for outpatient management we prefer giving oxazepam in dosages of 15 to 30 mg by mouth four times a day for five days. Phenothiazine and antihistamine ingestion should be avoided. Phenothiazines decrease the seizure threshold, and the acute anticholinergic effects of antihistamines and phenothiazines can confuse the clinical picture.

The treatment of seizures during alcohol withdrawal remains controversial. Patients who present in the early stages of alcohol withdrawal and who have no history of alcohol-withdrawal seizures are treated only with administration of sedative-hypnotics, as mentioned above. In patients with a history of alcohol-withdrawal seizures, one study has shown that prophylactic treatment with administration of sedative doses of chlordiazepoxide (up to 400 mg per day) plus phenytoin, 100

mg by mouth three times a day for five days, may be more effective than giving chlordiazepoxide alone.

In patients who present with alcohol-withdrawal seizures, our policy is to observe the character and frequency of the seizures. Most patients with alcohol-withdrawal seizures have two to six brief seizures in eight hours. If protected from injury and aspiration, they rarely suffer harm. For these reasons we recommend that anticonvulsant medication be withheld unless a patient has more frequent or prolonged seizures, focal seizures or status epilepticus. Focal seizures and status epilepticus require further workup. Long-term therapy with anticonvulsants given for alcohol-withdrawal seizures is not indicated as an underlying seizure focus does not exist.

Patients presenting with delirium tremens often have associated pulmonary and hepatic disease, dehydration and electrolyte disturbances. To treat these patients and search for other underlying disorders, intravenous administration of diazepam is the treatment of choice, with 10 mg given initially followed by 5 mg every five minutes. Once a "calm" state is induced, maintenance treatment with diazepam given by mouth may be instituted at a dosage of 5 to 20 mg every six hours.

Finally, other problems that are commonly associated with alcohol abuse must be sought out and treated in

a patient who has the withdrawal syndrome. These include problems with temperature regulation (hyperthermia or hypothermia), head injuries, alcoholic ketoacidosis, gastrointestinal bleeding, pancreatitis, hypoglycemia, thiamine deficiency and electrolyte disturbances such as hypokalemia and hypomagnesemia. Hypertension seen during alcohol withdrawal usually resolves in several days and need not be treated during withdrawal unless the patient is symptomatic or has a preexisting cardiac, renal or vascular disease.

Once the acute abstinence syndrome has been treated, plans for long-term rehabilitation should be initiated. Both drug (for example, disulfiram) and group therapy (Alcoholics Anonymous) have met with varying degrees of success and therefore a treatment regimen must be individualized for each patient.

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